REMARKS

Reconsideration is requested.

Claims 1-16, 18-21 and 23-28 are pending. Claims 6, 7 and 24-26 have been withdrawn from consideration. Claims 2-8, 17 and 22, have been canceled, without prejudice. Claims 1, 9-16, 18-21 and 23-28 will be pending upon entry of the present Amendment.

The claims have been amended, without prejudice. Support for the revisions may be found throughout the specification.

The Section 112, first paragraph "enablement", rejection of claims 27 and 28 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The cell derived from a part other than myocardium of an adult is defined in the rejected claims as an embryonic stem cell, a mesenchymal stem cell, a hematopoietic stem cell, a blood vessel stem cell, or a synovial cell. An embryonic stem cell is a pluripotent stem cell derived from early embryos (see ¶[0122] of the present specification).

A mesenchymal stem cell is included in tissue cells in the bone marrow and has abilities to proliferate and differentiate into bone cells, cartilage cells, muscle cells, stroma cells, tendon cells, and fat cells (see ¶¶[0122] and [0127] of the present specification).

Referring to Example 5 in the specification, it will be appreciated that synovial cells comprise tissue stem cells, the stem cells differentiate into the cells, which can

ameliorate cardiac function, and thereby the cell sheet of synovial cells ameliorated the cardiac function.

In view of the foregoing, for example, one of ordinary skill will appreciate that the embryonic stem cell, the mesenchymal stem cell, and synovial cells can differentiate into cardiac cell types.

In addition, the present specification states:

> "A 'disease' targeted by the present invention may be any heart disease in which tissue is injured. ... In a specific embodiment, a disease targeted by a method of the present invention is refractory heart failure" See ¶[0280].

The diseases recited in the claims commonly relate to injured tissue.

The specification further describes the following:

> "In addition to myocardial infarction, the cardiomyocyte sheet implantation method may be useful for repair of global myocardial dysfunction (e.g., dilated cardiomyopathy)" See ¶[0384] of the published specification.
>
> "A prosthetic tissue using newborn rat cardiomyocytes integrated with impaired myocardium and ameliorated cardiac function in an ischemic cardium model" See ¶[0395].
>
> "Therefore, it was demonstrated that when a myoblast sheet was implanted as a three-dimensional structure, the cardiac function of impaired myocardium was ameliorated" See ¶[0516] of the published specification.
>
> "Myoblast sheet implantation reduced the progression of heart hypertrophy with improvement of cardiac function in dilated cardiomyopathic (DCM) hearts. Myoblast sheet implantation may be a promising method to restore the cardiac function with attenuation of cardiac remodeling in DCM hearts" See ¶[0529] of the published specification.

Examples 4 to 6 also describe that each of a skeletal myoblast sheet, synovial cell sheet, and cardiomyocyte sheet ameliorates cardiac function in myocardial infarction.

The applicants submit that one of ordinary skill in the art will be able to make and use the claimed invention without requiring undue experimentation. Withdrawal of the Section 112, first paragraph, rejection is requested.

The Section 102 rejection of claims 1-5, 8-16, 18 and 23 over WO 01/07568 "as evidenced by" Carnac (1998, Mol. Biol. Cell., 9:1891-1902), is traversed. The Section 102 rejection of claims 1-5, 8, 11-17 and 19-23 over U.S. Patent No. 6,207,451 "as evidenced by" Carnac, is traversed. The Section 103 rejection of claims 27 and 28 over WO 01/07568 in view of Jin (Journal Pharm and Experimental Therapeutics, 02/01/2003, 304:654-660), is traversed. Reconsideration and withdrawal of the rejections are requested in view of the above and the following comments.

A three-dimensional structure of the claims will be recognized as a cell sheet, which is free from scaffold and obtained by using a temperature-responsive polymer.

The applicants submit that the cited WO 01/07568 describes that a transplantable muscle cell composition is not in the form of a cell sheet and is harvested by using 0.05% trypsin-EDTA (see page 12, lines 1 and 2).

In this connection, the present specification describes in ¶[0255] that

> "the prosthetic tissue and three-dimensional structure of the present invention is free from injury caused by a protein degrading enzyme, such as, representatively, dispase, trypsin, or the like, during culture ... When typical protein degrading enzymes (e.g. trypsin, etc.) are used to detach the three-dimensional structure or prosthetic tissue, substantially

> no desmosome structure between cell, basement membrane-like proteins between cells and base materials, or the like are retained, so that cells are individually separated"

A three-dimensional structure of the present disclosure has a structural difference not anticipated by the transplantable muscle cell composition described in WO 01/07568. Withdrawal of the Section 102 rejection is requested.

As note above, the three-dimensional structure of the present disclosure relates to a cell sheet obtained by using a temperature-responsive polymer. The cited U.S. Patent No. 6,207,451 describes a three-dimensional mammalian skeletal muscle construct (myooid) (column 3, lines 21 and 22). To form the construct, attachment of myogenic precursor cells to anchors is necessary (column 3, lines 52 to 54).

Further, Figure 3 of the cited patent shows a cross-section of a fully formed construct, that does not form a cell sheet.

Therefore, the three-dimensional structure of the present invention clearly has a structural difference from the construct described in the cited patent. Withdrawal of the Section 102 rejection over same is requested.

Claims 27 and 28 are patentable over WO 01/07568 in view of Jin. The secondary reference fails to cure the deficiencies of the primary reference, as described above. Jin is understood to describe, for example, that HGF may be beneficial to cardiovascular function. The reference fails to describe, for example, a three-dimensional structure of the present application or the combination of the structure with HGF. The methods of the rejected claims would not have been obvious in view of the cited combination of art. Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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